

CLAIMS

What is claimed is:

1. An isolated nucleic acid molecule encoding a gene product that, when knocked out, results in a high growth (*hg*) phenotype.
- 5 2. The nucleic acid of claim 1, wherein said nucleic acid comprises the nucleotide sequence of SEQ ID NO: 9.
3. The nucleic acid of claim 1, wherein said nucleic acid is present in a vector.
4. The nucleic acid of claim 1, wherein said nucleic acid is a DNA.
- 10 5. The nucleic acid of claim 1, comprising the nucleic acid or the complement of the nucleic acid of SEQ ID NO: 9.
6. A cell transfected with a nucleic acid molecule encoding a gene product that, when knocked out, results in a high growth (*hg*) phenotype.
7. The cell of claim 4, wherein said cell is a mammalian cell.
- 15 8. A method of producing an animal characterized by a high growth phenotype, said method comprising inhibiting expression of a *Socs2* gene.
9. The method of claim 8, wherein said inhibiting is by disrupting said gene by homologous recombination with a nucleic acid that undergoes homologous recombination with a *Socs2* gene and introduces a disruption in said *Socs2* gene.
- 20 10. The method of claim 9, wherein said nucleic acid encodes a selectable marker.
11. The method of claim 10, wherein said selectable marker is as *neo* or a *hyg* gene or cDNA.

12. A knockout mammal, said mammal comprising cells containing a recombinantly introduced disruption in a *Socs2* gene, wherein said disruption results in said knockout mammal exhibiting decreased levels of SOCS2 protein as compared to a wild-type mammal.

5 13. The knockout mammal of claim 12, wherein said mammal displays a high growth (hg) phenotype.

14. The knockout mammal of claim 12, wherein said mammal is selected from the group consisting of an equine, a bovine, a rodent, a porcine, a lagomorph, a feline, a canine, a murine, a caprine, an ovine, and a non-human primate.

10 15. The knockout mammal of claim 12, wherein, wherein the disruption is selected from the group consisting of an insertion, a deletion, a frameshift mutation, a substitution, and a stop codon.

15 16. The knockout mammal of claim 15, wherein, wherein said disruption comprises an insertion of an expression cassette into the endogenous *Socs2* gene.

17. The knockout mammal of claim 16, wherein, wherein said disruption comprises an expression cassette comprising a selectable marker.

20 18. The knockout mammal of claim 16, wherein the expression cassette comprises a neomycin phosphotransferase gene operably linked to at least one regulatory element.

19. The knockout mammal of claim 12, wherein said disruption is in a somatic cell.

20. The knockout mammal of claim 12, wherein said disruption is in a germ cell.

25 21. The knockout mammal of claim 12, wherein the mammal is homozygous for the disrupted *Socs2* gene.

22. The knockout mammal of claim 12, wherein the mammal is heterozygous for the disrupted *Socs2* gene.

23. The knockout mammal of claim 12, wherein said mammal further comprises a second recombinantly disrupted gene.

5 24. The knockout mammal of claim 23, wherein said second gene comprises a disruption that prevents the expression of a functional polypeptide from said disrupted second gene.

25. The knockout mammal of claim 23, wherein the mammal is homozygous for said disrupted second gene.

10 26. The knockout mammal of claim 23, wherein the mammal is heterozygous for said disrupted second gene.

27. A knockout rodent comprising a recombinantly introduced disruption in an endogenous SOCS2 gene (*Socs2*) wherein said disruption results in said knockout rodent exhibiting decreased levels of SOCS2 protein as compared to a wild-type
15 rodent.

28. The knockout rodent of claim 27, wherein said mammal displays a high growth (hg) phenotype.

29. The knockout rodent of claim 27, wherein, wherein the disruption is selected from the group consisting of an insertion, a deletion, a frameshift mutation, a
20 substitution, and a stop codon.

30. The knockout rodent of claim 27, wherein, wherein said disruption comprises an insertion of an expression cassette into the endogenous *Socs2* gene.

31. The knockout mammal of claim 30, wherein, wherein said disruption comprises an expression cassette comprising a selectable marker.

32. The knockout mammal of claim 30, wherein the expression cassette comprises a neomycin phosphotransferase gene operably linked to at least one regulatory element.

5 33. The knockout rodent of claim 27, wherein said disruption is in a somatic cell.

34. The knockout rodent of claim 27, wherein said disruption is in a germ cell.

35. The knockout rodent of claim 27, wherein the rodent is homozygous for the disrupted *Socs2* gene.

10 36. The knockout rodent of claim 27, wherein the rodent is heterozygous for the disrupted *Socs2* gene.

37. A method of screening for an agent that modulates expression of a high growth (hg) phenotype, said method comprising:

15 contacting a cell comprising a *Socs2* gene with a test agent; and
 detecting a change in the expression or activity of a *Socs2* gene product as compared to the expression or activity of a *Socs2* gene product in a cell that is contacted with the test agent at a lower concentration, where a difference in the expression or activity of *Socs2* in the contacted cell and the cell that is contacted with the lower concentration indicates that said agent modulates expression of a high growth phenotype.

20 38. The method of claim 37, wherein said lower concentration is the absence of said test agent.

39. The method of claim 37, wherein the amount of *Socs2* gene product is detected by detecting *Socs2* mRNA in said sample.

25 40. The method of claim 39, wherein said level of *Socs2* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *Socs2* nucleic acid.

41. The method of claim 40, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the *Socs2* RNA, an array hybridization, an affinity chromatography, and an in situ hybridization.

5 42. The method of claim 40, wherein said probe is a member of a plurality of probes that forms an array of probes.

43. The method of claim 39, wherein the level of *Socs2* mRNA is measured using a nucleic acid amplification reaction.

10 44. The method of claim 37, wherein the amount of *Socs2* gene product is detected by detecting the level of a *Socs2* protein in said biological sample.

45. The method of claim 37, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

46. The method of claim 37, wherein said cell is cultured *ex vivo*.

15 47. The method of claim 37, wherein said test agent is contacted to an animal comprising a cell containing the *Socs2* nucleic acid or the *Socs2* protein.

48. A method of prescreening for an agent that alters the expression of a high growth phenotype, said method comprising:

20 i) contacting a *Socs2* nucleic acid or a *Socs2* protein with a test agent; and
ii) detecting specific binding of said test agent to said *Socs2* protein or nucleic acid.

49. The method of claim 48, further comprising recording test agents that specifically bind to said *Socs2* nucleic acid or protein in a database of candidate
25 agents that alter *hg* phenotype development.

50. The method of claim 48, wherein said test agent is not an antibody.

51. The method of claim 48, wherein said test agent is not a protein.
52. The method of claim 48, wherein said test agent is not a nucleic acid.
53. The method of claim 48, wherein said test agent is a small organic
5 molecule.
54. The method of claim 48, wherein said detecting comprises detecting specific binding of said test agent to said *Socs2* nucleic acid.
55. The method of claim 54, wherein said binding is detected using a method selected from the group consisting of a Northern blot, a Southern blot using DNA
10 derived from a *Socs2* RNA, an array hybridization, an affinity chromatography, and an in situ hybridization.
56. The method of claim 48, wherein said detecting comprises detecting specific binding of said test agent to said *Socs2* protein.
57. The method of claim 48, wherein said detecting is via a method
15 selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.
58. The method of claim 48, wherein said test agent is contacted directly to the *Socs2* nucleic acid or to the *Socs2* protein.
59. The method of claim 48, wherein said test agent is contacted to a
20 cell containing the *Socs2* nucleic acid or the *Socs2* protein.
60. The method of claim 59, wherein said cell is cultured *ex vivo*.
61. The method of claim 48, wherein said test agent is contacted to an animal comprising a cell containing the *Socs2* nucleic acid or the *Socs2* protein.
62. An isolated nucleic acid comprising a nucleic acid selected from the
25 group consisting of:

a nucleic acid that specifically hybridizes to a nucleic acid selected from the group consisting of SEQ ID NO:2, and SEQ ID NO: 9 under stringent conditions; nucleic acid comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:2, and SEQ ID NO: 9.

5 63. The nucleic acid of claim 62, wherein said nucleic acid is at least 15 nucleotides in length.

64. A polypeptide comprising a polypeptide encoded by a nucleic acid of claim 62.

65. An antibody that specifically binds a polypeptide of claim 64.

10 66. A nucleic acid for disrupting a SOCS2 gene (*Socs2*), said nucleic acid comprising:

SOCS2 gene sequences that undergo homologous recombination with an endogenous SOCS2 gene: and

15 a nucleic acid sequence that, when introduced into a SOCS2 gene inhibits the expression of said SOCS2 gene.

67. The nucleic acid of claim 66, wherein said nucleic acid when introduced into a SOCS2 gene creates a disruption selected from the group consisting of an insertion, a deletion, a frameshift mutation, and a stop codon.

20 68. The nucleic acid of claim 66, wherein the disruption comprises the insertion of an expression cassette into the endogenous SOCS2 gene.

69. The nucleic acid of claim 66, wherein the expression cassette comprises a selectable marker.

70. The nucleic acid of claim 66, wherein said nucleic acid comprises *Socs2* nucleic acid sequences flanking a nucleic acid encoding a *Socs2* disruption.

25 71. The nucleic acid of claim 66, wherein said nucleic acid is present in a vector.

72. An animal cell comprising a recombinantly introduced disruption in an endogenous SOCS2 gene (*Socs2*) wherein said disruption results in said cell exhibiting decreased levels of SOCS2 protein as compared to a wild-type cell.

5 73. The cell of claim 72, wherein said cell of a animal is selected from the group consisting of a chicken, a turkey, a duck, a goose, an equine, a bovine, a rodent, a porcine, a lagomorph, a feline, a canine, a murine, a caprine, an ovine, and a non-human primate.

74. The cell of claim 72, wherein the cell is a rodent cell.

10 75. The cell of claim 72, wherein the disruption is selected from the group consisting of an insertion, a deletion, a frameshift mutation, and a stop codon.

76. The cell of claim 72, wherein the disruption comprises an insertion of an expression cassette into the endogenous SOCS2 gene.